

Application No. 10/588,679  
Amendment dated May 30, 2008  
Third Preliminary Amendment

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Docket No.: 62078(51590)

AMENDMENTS TO THE CLAIMS

1. (Currently amended) An isolated hMOR-1B1 splice variant polypeptide that consists essentially of the amino acid residues having the sequence of ~~SEQ ID NO:50~~ SEQ ID NO:51.
2. (Currently amended) An isolated hMOR-1B2 splice variant polypeptide that consists essentially of the amino acid residues having the sequence of ~~SEQ ID NO:52~~ SEQ ID NO:53.
3. (Currently amended) An isolated hMOR-1B3 splice variant polypeptide that consists essentially of the amino acid residues having the sequence of ~~SEQ ID NO:54~~ SEQ ID NO:55.
4. (Currently amended) An isolated hMOR-1B4 splice variant polypeptide that consists essentially of the amino acid residues having the sequence of ~~SEQ ID NO:56~~ SEQ ID NO:57.
5. (Currently amended) An isolated hMOR-1B5 splice variant polypeptide that consists essentially of the amino acid residues having the sequence of ~~SEQ ID NO:58~~ SEQ ID NO:59.
6. (Currently amended) An isolated hMOR-1Y splice variant polypeptide that consists essentially of the amino acid residues having the sequence of ~~SEQ ID NO:60~~ SEQ ID NO:61.
7. (Currently amended) The polypeptide as in claim 1 selected from the group consisting of SEQ ID NOs: 51, 53, 55, 57, 59, and 61 in which the polypeptide comprises a heterodimeric or homodimeric composition.

Application No. 10/588,679  
Amendment dated May 30, 2008.  
Third Preliminary Amendment

Docket No.: 62078(51590)

8. (Currently amended) An isolated polynucleotide, or an antisense-strand polynucleotide that is fully complementary thereto,-wherein the nucleotide fragment polynucleotide consists essentially of hMOR-1B1, having the sequence of ~~SEQ ID NO: 51~~ SEQ ID NO: 50.
9. (Currently amended) An isolated polynucleotide, or an antisense-strand polynucleotide that is fully complementary thereto,-wherein the nucleotide fragment polynucleotide consists essentially of hMOR-1B2, having the sequence of ~~SEQ ID NO: 53~~ SEQ ID NO: 52.
10. (Currently amended) An isolated polynucleotide, or an antisense-strand polynucleotide that is fully complementary thereto,-wherein the nucleotide fragment polynucleotide consists essentially of hMOR-1B3, having the sequence of ~~SEQ ID NO: 55~~ SEQ ID NO: 54.
11. (Currently amended) An isolated polynucleotide, or an antisense-strand polynucleotide that is fully complementary thereto,-wherein the nucleotide fragment polynucleotide consists essentially of hMOR-1B4, having the sequence of ~~SEQ ID NO: 57~~ SEQ ID NO: 56.
12. (Currently amended) An isolated polynucleotide, or an antisense-strand polynucleotide that is fully complementary thereto,-wherein the nucleotide fragment polynucleotide consists essentially of hMOR-1B5, having the sequence of ~~SEQ ID NO: 59~~ SEQ ID NO: 58.
13. (Currently amended) An isolated polynucleotide, or an antisense-strand polynucleotide that is fully complementary thereto,-wherein the nucleotide fragment polynucleotide consists essentially of hMOR-1Y, having the sequence of ~~SEQ ID NO: 61~~ SEQ ID NO: 60.
14. (Currently amended) A method of screening compositions for opioid activity comprising the steps of: a) obtaining a control cell that does not express an MOR-1 splice variant polypeptide; b) obtaining a test cell that is the same as the control cell except that it expresses an MOR-1 splice variant polypeptide as in claim 1 selected from the group consisting of SEQ ID NOS: 51, 53, 55, 57, 59, and 61; c) contacting the control cell and test cell with an amount of an opioid sufficient to exert a physiologic effect; d) separately measuring the physiologic effect of the composition on the control cell and test cell; and e)

Application No. 10/588,679  
Amendment dated May 30, 2008  
Third Preliminary Amendment

Docket No.: 62078(51590)

comparing the physiologic effect of the composition to the physiologic effect of the opioid, where determination of a physiologic effect of the composition is expressed relative to that of the opioid.

15. (Original) The method according to claim 14, where the composition is selected from the group consisting of synthetic combinatorial libraries of small molecule ligands, eukaryotic whole cell lysates or extracts, or media conditioned by cultured eukaryotic cells.
16. (Original) The method according to claim 14, where the opioid is selected from the group consisting of morphine, methadone, etorphine, levorphanol, fentanyl, sufentanil, [D-Ala<sub>2</sub>,MePhe<sub>4</sub>,Gly(ol)<sub>5</sub>]enkephalin, pentazocine, ethylketocyclazocine, bremazocine, spiradoline, [D-Ser<sub>2</sub>,Leu<sub>5</sub>]enkephalin-Thr<sub>6</sub>, Met-enkephalin, Leu-enkephalin, (3-endorphin, dynorphin A, dynorphin B, or  $\alpha$ -neoendorphin.
17. (Original) The method according to claim 14, where the physiological effect is measured by changes in the levels of neuroendocrine hormones.
18. (Original) The method according to claim 17, where the hormone is selected from the group consisting of prolactin, growth hormone, gonadotropin-releasing hormone, adrenocorticotropin, corticotropin-releasing factor, luteinizing hormone, follicle stimulating hormone, testosterone or cortisol.
19. (Currently amended) A method of screening compositions for opioid binding activity comprising the steps of: a) obtaining a control polypeptide that is not an MOR-1 splice variant polypeptide; b) obtaining a test polypeptide that is an MOR-1 splice variant polypeptide ~~as in claim 1~~ selected from SEQ ID NOs: 51, 53, 55, 57, 59, or 61 ; c) contacting a composition with the control polypeptide and the test polypeptide; d) contacting the test polypeptide with an amount of an opioid sufficient to measurably bind the test polypeptide; e) measuring the binding of the composition and the opioid; and f) comparing test polypeptide binding of the composition to that of the opioid, where determination of binding of the composition is expressed relative to that of the opioid.

Application No. 10/588,679  
Amendment dated May 30, 2008  
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Docket No.: 62078(51590)

20. (Original) The method according to claim 21 where the composition is selected from the group consisting of synthetic combinatorial libraries of small molecule ligands, eukaryotic whole cell lysates or extracts, or media conditioned by cultured eukaryotic cells.
21. (Currently amended) A method for regulating morphine analgesia in a subject comprising altering the amount of MOR-1 splice variant activity by: a) administering antigen binding fragments to a subject in an amount and a duration sufficient to regulate morphine analgesia; or b) administering agonists to a subject in an amount and a duration sufficient to regulate morphine analgesia; or c) administering antagonists to a subject in an amount and a duration sufficient to regulate morphine analgesia; or d) administering small molecule ligands to a subject in an amount and a duration sufficient to regulate morphine analgesia; or [(-d)] e) administering an antisense nucleic acid corresponding to a nucleic acid comprising a polypeptide encoding a polypeptide selected from the group consisting of a MOR-1 splice variant polypeptide fragment SEQ ID NOS: 51, 53, 55, 57, 59, and 61 or a homolog polypeptide fragment thereof or a polypeptide fragment thereof retaining MOR-1 opioid-binding activity, to a subject in an amount and a duration sufficient to regulate morphine analgesia; and wherein the antigen binding fragment, agonist, antagonist small molecule ligand or antisense nucleic acid is directed to an MOR-1 splice variant as in claim 1 selected from the group consisting of SEQ ID NOS: 51, 53, 55, 57, 59, and 61.